

DRAFT
Report on Carcinogens
Substance Profile for

Cobalt–Tungsten Carbide: Powders and Hard Metals



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Board of Scientific Counselors Meeting

This DRAFT substance profile contains the NTP's preliminary recommendation on the listing status of cobalt–tungsten carbide: powders and hard metals ~~glass wool fibers~~ in the Report on Carcinogens, summarizes the scientific information that supports the recommendation, and provides information on use, exposure, and production as well as any existing federal regulations.

This draft is distributed solely for the purpose of public comment and predissemination peer review and should not be construed to represent final NTP determination or policy.

Additional information about the NTP Report on Carcinogens review process for candidate substances is available at <http://ntp.niehs.nih.gov/go/29353>.

Revised June 22, 2010

Cobalt–Tungsten Carbide: Powders and Hard Metals

CAS No.: none assigned

Reasonably anticipated to be a human carcinogen

First listed in the *Twelfth Report on Carcinogens* (2010)

Also known as Co/WC, WC/Co

Carcinogenicity

Cobalt–tungsten carbide powders and hard metals are *reasonably anticipated to be human carcinogens* based on limited evidence of carcinogenicity from studies in humans and supporting studies on mechanisms of carcinogenesis.

Cancer Studies in Humans

Epidemiological studies provide evidence for the carcinogenicity of cobalt–tungsten carbide powders and hard metals based on (1) consistent findings of excess lung-cancer mortality among cobalt–tungsten carbide hard-metal manufacturing workers across studies, (2) higher risks among individuals with higher exposure levels, and (3) positive exposure-response relationships that cannot be explained by confounding with tobacco smoking. However, the epidemiological data are limited, because there are few studies of independent populations.

The published epidemiological literature consists of mortality studies of two independent multi-plant cohorts of cobalt–tungsten carbide hard-metal manufacturing workers, one in France (Moulin *et al.* 1998) and one in Sweden (Hogstedt and Alexandersson 1990), and cohort studies of two individual factories included in the French multi-plant cohort (Lasfargues *et al.* 1994, Wild *et al.* 2000). The French multi-plant cohort included all 10 cobalt–tungsten carbide manufacturing plants in France; in addition, a nested case-control study of lung cancer was conducted within this cohort. The nested case-control study is most informative for evaluating cancer risk, because it used a semi-quantitative exposure scale to evaluate exposure-response relationships and considered potential confounding by exposure to tobacco smoking and other known or suspected occupational carcinogens. The cohort study of the largest French factory shares these advantages; however, because the workers were included in the multi-plant study, it does not provide independent evidence for carcinogenicity. In these two studies, four metrics of exposure were evaluated: (1) exposure level, which was the highest exposure score experienced during an individual's work history (on a scale of 0 to 9), (2) duration of exposure at a level of 2 or higher, (3) unweighted cumulative dose, which assigned the same level to occasional and full-time exposure, thus favoring peak exposure, and (4) frequency-weighted cumulative dose, which weighted exposure level by the frequency of exposure, thus reducing the effect of occasional exposure. The Swedish study, although limited in size, provides supporting information for an independent population.

Excess lung-cancer mortality (of approximately 30%) was found in both multi-plant cohort studies (Hogstedt and Alexandersson 1990, Moulin *et al.* 1998); risk estimates

were significantly higher among individuals with higher measures of exposure or longer time since first exposure (latency). In the nested case-control study (Moulin *et al.* 1998), lung cancer risk was significantly higher (odds ratio [OR] = 1.93, 95% CI = 1.03 to 3.62, 35 exposed cases) among workers exposed to cobalt–tungsten carbide (exposure level ≥ 2) than among workers with little or no exposure (exposure level < 2). In exposure-response analyses using workers in the lowest exposure category as the comparison group, lung-cancer risk was significantly higher (by up to fourfold) for workers in the highest categories of both measures of cumulative dose, and an elevated risk of borderline statistical significance was found for workers in the highest exposure-level category. Positive exposure-response relationships were observed for all four measures of exposure: duration ($P_{\text{trend}} = 0.03$), unweighted cumulative dose ($P_{\text{trend}} = 0.01$), frequency-weighted cumulative dose ($P_{\text{trend}} = 0.08$), and exposure level ($P_{\text{trend}} = 0.08$). Adjustment for tobacco smoking or exposure to known or suspected carcinogens did not change the results. The Swedish study had limited ability to evaluate exposure-response relationships because of small numbers of exposed workers with lung cancer. Nevertheless, the risk of lung cancer mortality was significantly increased for workers with exposure duration of over 10 years and latency of over 20 years (standardized mortality ratio [SMR] = 2.78, 95% CI = 1.11 to 5.72, 7 exposed cases). Analyses restricted to workers with at least 10 years' exposure or at least 20 years' latency found somewhat higher SMRs for "high-exposed" than "low-exposed" workers (Hogstedt and Alexandersson 1990).

Excess risks of lung-cancer mortality were also found in studies of the two individual French factories. Wild *et al.* (2000) reported significantly elevated SMRs (by approximately twofold) for lung cancer among all male workers and among male workers ever employed in presintering workshops or with exposure levels of at least 2. The highest SMRs were observed for male workers in the highest exposure categories of all four exposure metrics (level, duration, and both measures of cumulative dose), although the trends were not statistically significant. In the study by Lasfargues *et al.* (1994), the entire cohort had a significantly increased risk of lung cancer, and the risk was highest among workers in the highest exposure-level category. Although small, this study provides supporting evidence that the findings for the French industry-wide cohort were not due solely to the results for the large factory studied by Wild *et al.*

Both the French multi-plant cohort study (Moulin *et al.* 1998) and the larger study of an individual French factory (Wild *et al.* 2000) found higher risks of lung cancer for exposure to cobalt–tungsten carbide before sintering than after sintering (see "Production"). The authors stated that exposure was highest during presintering processes; however, there is no evidence of toxicological differences between presintered and sintered materials, and both materials release similar amounts of cobalt ions (see "Studies on Mechanisms of Carcinogenesis").

It is unlikely that the excess risks of lung cancer found in the French studies were due to confounding by tobacco smoking or co-exposure to other known carcinogens. In the multi-plant study, the smoking-adjusted odds ratio for cobalt–tungsten carbide exposure (OR = 2.6, 95% CI = 1.16 to 5.82) was similar to the unadjusted risk (OR = 2.29, 95% CI = 1.08 to 4.88). Neither study found increased risks of smoking-related diseases, such as chronic bronchitis and emphysema, and adjustment for smoking or

exposure to other occupational carcinogens did not change the findings in the exposure-response analyses (Moulin *et al.* 1998, Wild *et al.* 2000). Neither the Swedish multi-plant study (Hogstedt and Alexandersson 1990) nor the small French cohort study (Lasfargues *et al.* 1994) adjusted for smoking; however, surveys of smoking habits among a subset of workers found smoking rates similar to those in the general population. Overall, the studies are limited by the lack of quantitative exposure assessment; however, exposure misclassification would most likely reduce the likelihood of detecting a true effect.

Studies on Mechanisms of Carcinogenesis

The findings from epidemiological studies are supported by studies on mechanisms of carcinogenesis. Although the mechanism(s) by which cobalt–tungsten carbide causes cancer have not been fully elucidated, it has been shown that (1) cobalt–tungsten carbide releases cobalt ions, (2) cobalt ions affect biochemical pathways related to carcinogenicity, (3) cobalt compounds are carcinogenic in experimental animals, (4) cobalt–tungsten carbide increases the production of reactive oxygen species (ROS) and causes greater cytotoxic, toxic, and genotoxic effects than does cobalt alone, (5) cobalt–tungsten carbide causes key events related to carcinogenesis, including genotoxicity, cytotoxicity, inflammation, and apoptosis (programmed cell death), and (6) the oxidative stress response resulting from increased ROS production may play a role in these key events and may also interfere with cells' ability to repair damage caused by cobalt–tungsten carbide. The combination of the effects from cobalt ions and the oxidative stress response from ROS production provide plausible modes of action for the carcinogenicity of cobalt–tungsten carbide.

Studies in biological fluids, *in vitro* systems, experimental animals, and humans have demonstrated that cobalt is rapidly solubilized from cobalt–tungsten carbide. Cobalt dissolution rates were similar for presintered and sintered cobalt–tungsten carbide incubated in various artificial biological fluids (Stopford *et al.* 2003). Cobalt was also released from hard-metal dust incubated with plasma and lung tissue (Edel *et al.* 1990). In experimental animals administered cobalt–tungsten carbide by intratracheal administration, cobalt was solubilized rapidly, cleared from the lung, distributed in the body, and excreted in the urine (reviewed by Lison 1996). Rats exposed intratracheally to cobalt–tungsten carbide had more cobalt in the urine than did rats administered cobalt alone, suggesting that tungsten carbide increases the bioavailability of cobalt (Lasfargues *et al.* 1992). Several biomonitoring studies detected elevated levels of cobalt in the urine, lungs, and other tissues of workers exposed to cobalt–tungsten carbide hard metals (Gallorini *et al.* 1994, Goldoni *et al.* 2004, Linnainmaa and Kiilunen 1997, Sabbioni *et al.* 1994a, Scansetti *et al.* 1994, 1998, Rizzato *et al.* 1986, Nicolaou *et al.* 1987).

Soluble cobalt compounds are genotoxic and carcinogenic in experimental animals. Cobalt sulfate is listed as *reasonably anticipated to be a human carcinogen* in the Report on Carcinogens based on sufficient evidence of carcinogenicity from studies in experimental animals. Specifically, inhalation exposure to cobalt sulfate in rodents caused lung tumors (adenoma or carcinoma) in mice and rats and adrenal-gland tumors (pheochromocytoma) in female rats (Bucher *et al.* 1999). Cobalt ions produce ROS, which cause oxidative DNA damage and act on a number of cancer-related molecular

targets. Cobalt ions disrupt cell-signaling pathways (Murata *et al.* 1999), inhibit DNA repair (Hartwig 2000, Hartwig *et al.* 2002), regulate genes involved in the response to hypoxia (Beyersmann 2002), replace or mimic essential divalent metal ions thus altering cellular reactions (Nackerdien *et al.* 1991, Beyersmann and Hartwig 1992, Kawanishi *et al.* 1994, Lloyd *et al.* 1998), and interfere with mechanisms involved in cell-cycle control and modulation of apoptosis (De Boeck *et al.* 2003a,b).

Numerous *in vitro* studies (reviewed in NTP 2009) and *in vivo* studies (Huaux *et al.* 1995, Lasfargues *et al.* 1995) have shown greater cytotoxic effects (measured primarily by lactate dehydrogenase release) for cobalt–tungsten carbide than for either cobalt powder or tungsten carbide alone. The mixture’s greater *in vitro* toxicity to macrophages is not fully explained by greater bioavailability of cobalt (Lison and Lauwerys 1992, 1994). Respirable samples collected at various stages of the hard-metal manufacturing process (including powders for pressing, presintered materials, and powders from grinding of sintered materials) caused cytotoxicity and pathological changes in the lungs of rats after intratracheal injection (Adamis *et al.* 1997). In addition, cobalt–tungsten carbide causes a type of respiratory toxicity (“hard-metal disease”) that is not observed with exposure to cobalt alone. Hard-metal disease is characterized by a giant-cell interstitial pneumonia that can develop into lung fibrosis (Lison 1996, Lison *et al.* 1996).

There is some evidence that the greater toxicity of cobalt–tungsten carbide may result from a physicochemical reaction that takes place at the interface between certain carbides and cobalt particles (Lison and Lauwerys 1992). The structural features of the two particles may help to explain the effects. Cobalt metal can reduce ambient oxygen, but only at a low rate of reaction because of the particles’ surface characteristics. Tungsten carbide is inert and does not react with oxygen but is a good electron conductor. When cobalt and tungsten carbide particles are associated, the cobalt electrons are transferred to the carbide surface, allowing increased oxygen reduction and thus increased production of ROS. Biochemical studies on the production of ROS have shown that cobalt’s capacity to generate hydroxyl radicals is greatly increased by association with tungsten carbide. Formation of the ROS results directly from the interaction of cobalt with tungsten carbide or indirectly from the cobalt ions generated from the Fenton-like reaction of the cobalt metal with the carbide (Lison and Lauwerys 1993, Lison *et al.* 1995).

Metal-induced generation of ROS in cellular test systems leads to oxidative stress as a result of increased free radicals and insufficient antioxidative defense. Protective mechanisms include cellular antioxidant systems, the stress-protein response, and the involvement of DNA excision and repair enzymes (Kasten *et al.* 1997, Shi *et al.* 2004, Lombaert *et al.* 2008). Fenoglio *et al.* (2008) studied oxidation of the antioxidant glutathione and cysteine sulfhydryl groups by cobalt–tungsten carbide dust–induced ROS and reported dust-concentration-dependent generation of thiyl radicals at particle surface sites. Depletion of cellular antioxidant defenses could further exacerbate cellular oxidative damage caused by ROS generated by cobalt–tungsten carbide particles.

Regulation of gene expression, including apoptotic, stress-protein, and immune-response pathways, also can be affected by ROS. Lombaert *et al.* (2008) evaluated the effects of cobalt–tungsten carbide exposure *in vitro* on patterns of gene expression in

human peripheral-blood mononucleated cells and reported statistically significant up-regulation of apoptosis and stress or defense response pathways and down-regulation of immune-response pathways.

Apoptosis has been associated with exposure to a number of metals that are either known carcinogens (arsenic, cadmium, chromium, nickel, beryllium) or possible carcinogens (cobalt, lead) (Pulido and Parrish 2003). Cobalt chloride has been shown to induce apoptosis through formation of ROS in both human alveolar macrophages and a rat pheochromocytoma cell line (PC12); co-administration of antioxidants suppressed ROS production and restored cell viability (Zou *et al.* 2001, Araya *et al.* 2002). Cobalt–tungsten carbide, tungsten carbide, and cobalt ions induced apoptosis in human lymphocytes; the effect of the mixture was significantly greater than that of tungsten carbide or cobalt alone (Lombaert *et al.* 2004).

Cobalt–tungsten carbide is genotoxic *in vitro* and causes mutations in the lungs of rats exposed *in vivo*. Its genotoxicity (clastogenic effects) may be caused by increased ROS production from the interaction between cobalt and tungsten carbide, from ionic cobalt, or from both. In addition, cobalt ions inhibit DNA repair, which may also contribute to cobalt–tungsten carbide’s genotoxic effects. Specifically, cobalt–tungsten carbide caused DNA strand breaks in mouse 3T3 fibroblasts and human peripheral-blood lymphocytes (Anard *et al.* 1997) and micronucleus formation in human peripheral-blood lymphocytes (Van Goethem *et al.* 1997, De Boeck *et al.* 2003a). In these studies, cobalt–tungsten carbide was more genotoxic than cobalt alone. In rats exposed by intratracheal instillation, cobalt–tungsten carbide caused DNA damage and micronucleus formation in the lung (type II pneumocytes) (De Boeck *et al.* 2003c). In humans, neither DNA damage nor micronucleus formation was increased in lymphocytes of cobalt–tungsten carbide hard-metal workers, compared with unexposed workers; however, this study was limited by small sample size (De Boeck *et al.* 2000). Multiple regression analyses (Mateuca *et al.* 2005) indicated that both end points were associated with an interaction between tobacco smoking and exposure, and that micronucleus formation was associated with smoking, working in a cobalt–tungsten carbide plant, and having variant forms of genes coding for DNA repair enzymes (X-ray repair cross-complementing group 3 and 8-oxoguanine DNA glycosylase).

In addition, although the pathogenesis of hard-metal disease is not fully understood, it may involve differences in the susceptibility (genetic and/or health-related) of affected individuals to the toxic effects of increased ROS production due to cobalt–tungsten carbide exposure. Further, the mechanisms for fibrosing alveolitis and lung cancer in hard-metal workers may be related, conceivably involving oxidative damage and/or inflammatory events (IARC 2006).

Cancer Studies in Experimental Animals

No studies in experimental animals were identified that evaluated the relationship between cancer and exposure specifically to cobalt–tungsten carbide powders or hard metals.

Properties

This listing includes powders and dusts (either unsintered or sintered) containing both cobalt and tungsten carbide and hard metals containing both cobalt and tungsten carbide. Powders containing both cobalt and tungsten carbide may result from combination of these materials during manufacture of hard metals, and dusts containing both materials may result from production, finishing, or maintenance (e.g., sharpening or grinding) of cobalt–tungsten carbide hard-metal products. Cobalt–tungsten carbide hard metals are composites of tungsten carbide particles (either alone or in combination with smaller amounts of other carbides) with a metallic cobalt powder as a binder, pressed into a compact, solid form at high temperatures by a process known as “sintering.” Cobalt–tungsten carbide hard metals are commonly referred to as “cemented carbides” in the United States, but the term “sintered carbide” also may be used, and some sources refer to cobalt–tungsten carbide products simply as “tungsten carbides” (Brookes 2002).

The physical properties of cobalt–tungsten carbide hard metals vary with the relative proportions of cobalt, tungsten carbide, and other carbides, but they have common properties of extreme hardness, abrasion resistance, and toughness. Tungsten carbide is hard (able to resist cutting, abrasion, penetration, bending, and stretching) but brittle; cobalt is soft but tough (able to withstand great strain without tearing or breaking). The composition of commercial-grade cobalt–tungsten carbide hard metals can vary greatly; it generally ranges from 50% to 97% tungsten carbide (along with other metallic carbides such as titanium carbide or tantalum carbide) and from 3% to 16% cobalt, with variations in grain size and additives. The proportion of cobalt as the binding metal in the composite hard metal depends on the intended use (Azom 2004). Cobalt–tungsten carbide hard metals for various uses have Vickers hardness values (a measure of the resistance of a substance to indentation by a diamond penetrator of special profile) typically ranging from 1250 to 1900 (Brookes 1998).

Mixtures of cobalt and tungsten carbide are more active than the individual components in adsorption of water vapor (with respect to both the amount adsorbed and the interaction energy) and in the catalytic decomposition of hydrogen peroxide (Zanetti and Fubini 1997). Physical and chemical properties of tungsten carbide and cobalt are listed in the following table.

Property	Tungsten carbide ^a	Cobalt ^b
Molecular or atomic weight	195.9	58.9
Density/specific gravity	15.6	8.92
Melting point	2,785°C	1,495°C
Boiling point	6,000°C	2,927°C
Vapor pressure	NA	1 Pa at 1,517°C (0.0075 mmHg)

Sources: ^aHSDB 2010a, ^bHSDB 2010b. NA = Not available.

Use

Approximately 70% of cobalt–tungsten carbide hard-metal production is used for cutting tools and 30% for wear-resistant materials, primarily for tools for mining and grinding operations (Kirk-Othmer 1997). Hard-metal grades for machining are assigned International Organization for Standardization (ISO) codes beginning with “P” for machining of steel, “M” for multiple purposes, including machining of steel, nickel-based superalloys, and ductile cast iron, and “K” for cutting of gray cast iron, nonferrous metals, and nonmetallic materials.

Production

Cobalt–tungsten carbide hard metals were developed in Germany during and after World War I and marketed commercially by a German company in 1927 as Widia, which consisted of tungsten carbide with 6% cobalt as binder (Brookes 1998, Upadhyaya 1998). Cobalt–tungsten carbide hard-metal manufacturing processes vary somewhat, but all involve production of cobalt and tungsten carbide powders, which are mixed, pressed into a compact, solid form, and heated to approximately 1,500°C — a process known as “sintering.” The manufacturing process consists of three steps: Step 1, producing the cobalt and tungsten carbide powders; Step 2, mixing, drying, pressing, presintering, shaping the presintered hard metal, and sintering; and Step 3, finishing the sintered products.

Worldwide use of cemented carbides has increased steadily over the years, from about 10 tons in 1930 to 30,000 tons per year in the early 2000s (Azom 2004). In 2004, estimated U.S. production of hard-metal products totaled 5,527 metric tons (6,080 tons) (Hsu 2004). The United States Geological Survey (USGS 2008a,b) estimated that 792 metric tons (873 tons) of cobalt (9.3% of total U.S. cobalt consumption) and 6,610 metric tons (7,286 tons) of tungsten (56% of total U.S. tungsten consumption) were used in the production of cemented carbides in the United States in 2007. The Thomas Register (ThomasNet 2008) identified 127 U.S. and Canadian companies that produced or supplied cobalt–tungsten carbide and materials made from cobalt–tungsten carbide. In 2008, the Cemented Carbide Producers Association had 22 U.S. members or partner members (CCPA 2008). In 2007, the United States exported approximately 1.3 million kilograms (1,427 tons) and imported approximately 1.6 million kilograms (1,778 tons) of tungsten carbide (USITC 2008); no data specific to cobalt–tungsten carbide were found.

Exposure

The major source of exposure to cobalt–tungsten carbide powders and hard metals is occupational. However, people who live in the vicinity of hard-metal production or maintenance facilities could be exposed to cobalt–tungsten carbide hard-metal dusts. Although no exposure levels for the general public were found, some studies provided data on possible environmental contamination from the manufacture or maintenance of hard-metal products. Soil sampled from the rear of a cemented carbide tool-grinding plant contained cobalt at concentrations of up to 12,780 mg/kg (Abraham and Hunt 1995). The concentrations of tungsten and cobalt in airborne particulates in Fallon, NV

and four nearby towns were characterized by Sheppard *et al.* (2006), and the levels of tungsten (0.1 to 40.9 ng/m³) and cobalt (0.02 to 0.16 ng/m³) were reported to be higher in Fallon than in the other towns. Sheppard *et al.* suggested that a hard-metal facility located in Fallon could be a candidate source for the airborne exposure to the metals, although that suggestion has been disputed (NTP 2009).

Sources of occupational exposure to cobalt–tungsten carbide during the manufacture of hard metals include the Step 2 processes of mixing, drying, pressing, presintering, shaping, and sintering and Step 3 processes of grinding and sharpening sintered products. Exposure to cobalt–tungsten carbide hard metals can also occur from other miscellaneous manufacturing operations, during processing of hard-metal scrap for recycling, and during end use and maintenance of hard-metal tools. Cobalt and tungsten have been detected in workers' urine, blood, hair, toenails, and bronchoalveolar lavage fluid, and through open lung and transbronchial biopsy.

Step 2 processes, particularly powder-processing operations, generally are associated with the highest airborne exposures; several studies reported cobalt concentrations exceeding 5,000 µg/m³ (NTP 2009). A maximum mean cobalt air concentration of 32,740 µg/m³ (range = 44 to 438,000 µg/m³) was reported during weighing and mixing operations in a U.S. manufacturing facility (Sprince *et al.* 1984). An Italian study reported a mean tungsten air concentration of 26 µg/m³ (Sabbioni *et al.* 1994b), and a German study reported a maximum single measurement of 254 µg/m³ (Kraus *et al.* 2001). Among workers involved in Step 2 manufacturing processes, cobalt was detected in the urine (at up to 2,100 µg/L), blood or serum (at up to 32 µg/L), and hair (at up to 25.8 ppm), and tungsten was detected in urine (at up to 169 µg/L).

Cobalt air concentrations reported for Step 3 processes (including tool finishing, grinding, and reconditioning operations) have generally been lower than those for Step 2, but have exceeded 1,000 µg/m³ in some studies (NTP 2009). For Step 3 processes, a maximum mean cobalt air concentration of 1,292 µg/m³ and a maximum single measurement of 2,440 µg/m³ were reported; both concentrations were for dry-grinding operations. For tungsten in air, a maximum mean concentration of 5,160 µg/m³ and a maximum single measurement of 12,800 µg/m³ were reported. Among workers involved specifically in Step 3 processes, cobalt was detected in urine (at up to 730 µg/L), blood (at up to 39 µg/L), and hair (at up to 9.11 ppm). Tungsten also was detected in urine (up to 1,000 µg/L) and blood (up to 60 µg/L).

A few studies reported on exposure for jobs outside of the cobalt–tungsten carbide production process. McDermott (1971) reported airborne cobalt concentrations during packing operations (10 to 250 µg/m³), equipment cleaning (40 to 820 µg/m³), and miscellaneous operations (10 to 6,700 µg/m³), but the nature of these operations was not defined further. Maintenance activities (including housekeeping) were reported by Scansetti *et al.* (1985) to result in airborne cobalt concentrations exceeding 50 µg/m³, and Kraus *et al.* (2001) reported urinary levels associated with maintenance activities ranging from 1.3 to 4.7 µg/L for cobalt and 1.5 to 5.3 µg/L for tungsten.

Information on exposure from end use of hard-metal tools is limited. Pellet *et al.* (1984, as cited in Angerer and Heinrich 1988) reported cobalt air concentrations of 180 to 193 µg/m³ and a mean urinary cobalt concentration of 11.7 µg/L associated with use of

hard metal; however, no additional information was provided for these data. No other information was found that directly demonstrated exposure to cobalt–tungsten carbide powders and hard metals by end users of products containing the material. The Washington State Department of Labor, in a Hazard Alert issued in March 1995, stated that there was no evidence of substantial exposure to cobalt during the use of tools containing tungsten carbide or other hard metals (WSDLI 1995).

Several studies found significant correlations between cobalt concentrations in air and in workers' blood or urine (Ichikawa *et al.* 1985, Scansetti *et al.* 1985, Lison *et al.* 1994, Sabbioni *et al.* 1994b). Urinary cobalt levels for hard-metal workers have been reported to increase through the workday (Torra *et al.* 2005) and workweek (Lison *et al.* 1994, Scansetti *et al.* 1998, Torra *et al.* 2005). In one study, urinary cobalt concentrations were significantly higher ($P < 0.005$) at the end of a shift than at the beginning of the shift, with significant increases “day in and day out” during the workweek (Torra *et al.* 2005).

Regulations

U.S. Environmental Protection Agency (EPA)

Clean Water Act

Tungsten and cobalt discharge limits are imposed for numerous processes during the production of tungsten or cobalt at secondary tungsten and cobalt facilities processing tungsten or tungsten carbide scrap raw materials.

Discharge limits for tungsten are imposed for numerous processes during the production of tungsten at primary tungsten facilities.

Discharge limits for cobalt are imposed for numerous processes during the production of cobalt at primary cobalt facilities.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Cobalt and cobalt compounds are listed substances subject to reporting requirements.

Occupational Safety and Health Administration (OSHA)

Permissible exposure limits (PEL): for cemented tungsten carbide containing $> 2\%$ Co (as Co) = 0.1 mg/m^3 (8-hour TWA); for cobalt metal, dust, and fume (as Co) = 0.1 mg/m^3 ; for insoluble tungsten compounds (as W) = 5 mg/m^3 ; for soluble tungsten compounds (as W) = 1 mg/m^3 .

Short-term exposure limits (STEL): for insoluble tungsten compounds (as W) = 10 mg/m^3 ; for soluble tungsten compounds (as W) = 3 mg/m^3 .

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) for cobalt and inorganic cobalt compounds = 0.02 mg/m^3 ; for tungsten metal and insoluble compounds = 5 mg/m^3 .

Threshold limit value – short-term exposure limit (TLV-STEL) for tungsten metal and insoluble compounds = 10 mg/m^3 ; for soluble tungsten compounds = 3 mg/m^3 .

Biological exposure index (BEI): for cobalt in urine = $15 \text{ } \mu\text{g/L}$ end of shift at end of workweek; for cobalt in blood = $1 \text{ } \mu\text{g/L}$ end of shift at end of workweek.

National Institute for Occupational Safety and Health (NIOSH)

Recommended exposure limit (REL) (10-hour TWA): for cemented tungsten carbide containing $> 2\%$ Co (as Co) = 0.05 mg/m^3 ; for cobalt metal dust and fume (as Co) = 0.05 mg/m^3 ; for tungsten and insoluble tungsten compounds (as W) = 5 mg/m^3 ; for soluble tungsten compounds (as W) = 1 mg/m^3 .

Immediately dangerous to life and health (IDLH) limit for cobalt metal dust and fume (as Co) = 20 mg/m^3 .

Short-term exposure limit for tungsten and insoluble tungsten compounds (as W) = 10 mg/m^3 ; for soluble tungsten compounds (as W) = 3 mg/m^3 .

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